

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	MDL No. 2875
THIS DOCUMENT RELATES TO ALL CASES	HON. ROBERT B. KUGLER CIVIL NO. 19-2875 (RBK)(KMW)

**PLAINTIFFS' BRIEF IN OPPOSITION TO DEFENDANTS'
MOTION TO EXCLUDE THE GENERAL CAUSATION
TESTIMONY OF PLAINTIFFS' EXPERT DAVID MADIGAN, PH. D.**

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PRELIMINARY STATEMENT

Dr. Madigan is a Doctor of Mathematics and Biostatistics, who has repeatedly qualified to testify in federal courts. Dr. Madigan was retained by Plaintiffs to analyze the underlying data in epidemiological studies related to NDMA or NDEA and cancer risk, and calculate the lifetime cumulative NDMA or NDEA exposures associated with the cancer risk. The epidemiological studies analyzed by Dr. Madigan utilized various scientifically recognized methods of data retrieval and analysis. The collection of literature Dr. Madigan reviewed included both human dietary and occupational exposure studies which quantified NDMA and/or NDEA exposure.

Dr. Madigan began with the comprehensive epidemiological literature compiled by Plaintiffs' epidemiologist, Dr. Etminan. (Madigan Dep. at 198:9-14, attached hereto as **Exhibit A**). Then, in an attempt to pinpoint any additional studies that quantified the amounts of NDEA and NDMA, Dr. Madigan independently conducted his own literature search and investigated the articles referenced within each piece of literature identified by Dr. Etminan. (Madigan Dep. at 71:6-15; 196:18-20; 265:7-14). Dr. Madigan was unable to identify any additional epidemiological studies that ascertained NDMA or NDEA exposure to a reasonable degree of accuracy. (Madigan Dep. at 71:16). Dr. Madigan and Dr. Etminan identified numerous epidemiological studies, both dietary and occupational, that sufficiently quantified the amounts of NDMA or NDEA to which the study participants were exposed. For each identified study, Dr. Madigan performed a statistical analysis to evaluate the strength of association¹ and any potential dose response.² Additionally, Dr. Madigan calculated the mean "lifetime cumulative

¹ Strength of association refers to the strength of a relationship between two separate variables.

² Dose response refers to the observation that as the dose of an exposure increases, the outcome (in this case cancer formation) increases. A positive dose response significantly increases the strength of association.

exposure” (LCE)³ to NDMA or NDEA in each study, to enable further comparison of the studies to Plaintiffs. After performing his statistical analysis, Dr. Madigan determined that the vast majority of studies indicate an increased risk of cancer due to NDMA or NDEA. Dr. Madigan presented his findings for all studies, irrespective of each study’s outcome.

I. THE DAUBERT STANDARD

Federal Rule of Evidence 702 requires trial courts to “ensure that any and all scientific testimony ... is not only relevant, but reliable.” *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 147, 119 S. Ct. 1167, 1174, 143 L. Ed. 2d 238 (1999) (internal citations omitted). This standard applies to all expert testimony, not just scientific testimony. *Id.* The trial courts have a role of gatekeeper when screening expert testimony. *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 142, 118 S. Ct. 512, 517, 139 L. Ed. 2d 508 (1997). This Circuit has liberally interpreted FRE 702 in favor of admissibility. *Holbrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 781 (3d Cir. 1996).

FRE 702 has three requirements: 1) that the offered witness be an expert, 2) that the expert testify about matters using their scientific, technical, or specialized knowledge, and 3) that the testimony assist the trier of fact. *Kannankeril v. Terminix Int’l, Inc.*, 128 F.3d 802, 806 (3d Cir. 1997), *as amended* (Dec. 12, 1997). Regarding the second prong, an expert’s opinion will be held to be admissible as long as the process or technique the expert used in formulating the opinion is reliable, which requires that the testimony be based on “methods or procedures of science” rather than on “subjective belief or unsupported speculation.” *Id.* (internal citations omitted). Admissibility determinations are based on the expert’s methods and reasoning, with credibility decisions decided after admissibility has been determined. *Id.* Offerors of an expert

³ Lifetime cumulative exposure determines one’s total amount of exposure to NDMA or NDEA based on the daily dose of exposure and the duration of exposure.

witness must prove by a preponderance of the evidence that the expert's opinions are based on good grounds. *Id* at 807.

Expert "knowledge" in this context connotes more than "subjective belief or unsupported speculation" but is rather applied to any body of known facts or to any body of ideas inferred from such facts or accepted as truths on good grounds." *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 590, 113 S. Ct. 2786, 2795, 125 L. Ed. 2d 469 (1993). This does not mean that an expert can only opine on matters "known" to a certainty, as there are arguably no certainties in science. *Id*. Unlike an ordinary witness, an expert is permitted wide latitude to offer opinions, "including those that are not based on firsthand knowledge or observation." *Id* at 592.

II. DR. MADIGAN'S OPINIONS SHOULD BE ADMITTED

1. Dr. Madigan's Opinions on Strength of Association, Dose Response, and Lifetime Cumulative Exposure All Speak to General Causation

Defendants claim that all of Dr. Madigan's opinions should be excluded on the premise that Dr. Madigan lacks the qualifications to give general causation opinions. Dr. Madigan is not giving a general causation opinion in this case. He is providing statistics based expert testimony. Defendants incorrectly state the standard for admission of statistics-based expert testimony, misrepresent Dr. Madigan's statistical opinion as a medical one, and frame multiple cases in which Dr. Madigan's statistical opinion was allowed as a basis for excluding his statistical opinion here. Defendants also erroneously state that Dr. Madigan devalues the strength of association. Dr. Madigan is a highly qualified statistician and numerous courts have permitted him to provide opinions based on his statistical expertise in the area of biostatistics and analysis. Dr. Madigan's expert testimony meets all of the current standards for expert testimony under the Federal Rules of Evidence and his testimony should be admitted.

a. Dr. Madigan is Not Providing a Full General Causation Opinion, and is Well Qualified to Offer his Biostatistical Analysis

Defendants claim that because Dr. Madigan is not offering a standalone general causation opinion, his opinions are irrelevant and should be excluded. (Def. Br. at 3-4; 10-11, attached hereto as **Exhibit R**). However, Dr. Madigan's opinions on dose response, strength of association, and lifetime cumulative exposure provide additional support and insight into the studies that underly the general causation opinions of Plaintiffs' experts.

Defendants allege that a partial general causation opinion should not be admitted. However, New Jersey Federal Courts have permitted this very thing. In outlining the Daubert standard, the District Court of New Jersey noted that "an expert opinion is not inadmissible because it may contain flaws, **nor is it excludable because it provides testimony regarding only one facet or aspect of an action but does not prove the whole case**; such vulnerabilities affect the weight of the testimony, not its admissibility." *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Practices & Prods. Litig.*, 509 F. Supp. 3d at 131 (D.N.J. 2020) (citing *Feit v. Great-W. Life & Annuity Ins. Co.*, 460 F. Supp. 2d 632, 641 (D.N.J. 2006)). Further, in the *Talcum* decision cited above, plaintiff's expert Dr. Saed was permitted to testify to his opinions on the association between talc use and cellular oxidative stress, which was only one part of the plaintiffs' expert proof on general causation. *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Practices & Prods. Litig.*, 509 F. Supp. 3d at 140-141. This demonstrates that an expert is permitted to provide reliable opinions that underly general causation, but are not general causation opinions themselves.

With regard to Dr. Madigan specifically, Defendants cite *Abilify* in their brief as basis for excluding Dr. Madigan's expert opinions. Defendants' reliance on *Abilify* is unpersuasive, as the bulk of Dr. Madigan's expert opinions were actually admitted by the court. *In re Abilify*

(*Aripiprazole*) *Prod. Liab. Litig.*, 299 F. Supp. 3d 1291, 1361 (N.D. Fla. 2018). While it is true that the Court excluded any medical or scientific opinions related to the causation of gambling and impulse control disorder, because Dr. Madigan admitted a lack of expertise in these areas, the court ultimately concluded that “Dr. Madigan [is] **amply qualified** to offer a **biostatistical analysis** of the evidence in this case, as well as opinions related to pharmacovigilance and clinical trials generally, as **his credentials in these fields are well beyond reasonable challenge.**” *In re Abilify* 299 F. Supp. 3d at 1361 (emphasis added).

Just as in *Abilify*, Dr. Madigan is only offering a biostatistical analysis of the evidence in this case, including strength of association, dose response, and lifetime cumulative exposures. Dr. Madigan is not offering any medical causation opinions in this case, and Defendants’ argument to exclude any of Dr. Madigan’s opinions on such a basis is improper.

Defendant’s reliance on the unpublished *In re Vioxx Prod. Liab. Litig.* decision is similarly unpersuasive. The court in *Vioxx* held that Dr. Madigan would be disallowed from offering opinions on “Merck’s actions or inactions in disclosing or not disclosing various results. Similarly, Dr. Madigan should not offer opinions regarding Merck’s interpretations of the test results” because “such testimony would be outside his field of expertise, and therefore inadmissible under the *Daubert* standard.” *In re Vioxx Prod. Liab. Litig.*, No. MDL 1657, 2016 WL 8711273, at *4 (E.D. La. Sept. 16, 2016) (attached hereto as **Exhibit K**). However, the court held that his opinions regarding statistical analysis of the data would be admitted, stating:

Dr. Madigan does have **extensive experience with mathematics and statistics**. Therefore, if he is tendered as an expert his testimony and opinions should be related to these fields. **He may offer opinions regarding the field of statistics, how they are compiled, and their general use.**

Id. (emphasis added).

The only cases Defendants cite as a basis for excluding Dr. Madigan from offering opinions related to general causation, *Abilify* and *Vioxx*, both permitted Dr. Madigan's statistical analysis of the underlying data for the exact same purpose Dr. Madigan's statistical analysis is offered here: to provide additional context and insight into the underlying basis for general causation.⁴ Dr. Madigan offers his statistical analysis of the relevant data, a task for which he is amply qualified, as has been recognized by numerous courts.

b. Dr. Madigan's Strength of Association Opinions Utilize Well-Established Scientific Methodology and are Relevant to General Causation

Defendants attempt to diminish the relevance of Dr. Madigan's strength of association opinions, despite the fact that these opinions are recognized by both the scientific community and the courts as a reliable method of forming general causation opinions. The court in *Viagra* properly recognized that "the Bradford Hill criteria are used to establish general causation from epidemiological studies—they are not used to establish specific causation." *In re Viagra Prod. Liab. Litig.*, 658 F. Supp. 2d 950, 958 (D. Minn. 2009) (internal citations omitted). Strength of association is one of many Bradford Hill criteria.⁵ Defendants claim that Dr. Madigan's finding of a "statistically significant association" between "lifetime cumulative exposure" to dietary and

⁴ In their motion to exclude Dr. Etminan, Defendants incorrectly claim that Dr. Etminan's opinions "do not fit this case" because he relies on studies where dose and duration (cumulative exposure) of NDMA or NDEA exposure significantly exceed the cumulative exposures of Plaintiffs due to contaminated valsartan. (Def. Etminan Br. at 1). Dr. Madigan's statistical analysis provides further support that the epidemiological studies underlying Dr. Etminan's general causation opinions are applicable to contaminated valsartan users, since Plaintiffs ingesting NDMA contaminated valsartan will reach and exceed the cumulative NDMA or NDEA exposures in those studies.

⁵ "Developed by Sir Bradford Hill in the 1960s, the criteria are nine factors which researchers often consider when judging whether an observed association is truly causal. The Bradford Hill criteria are: 1) strength of association; 2) consistency; 3) specificity of the association; 4) temporality; 5) dose-response curve; 6) biological plausibility; 7) coherence (with other knowledge); 8) experiment; and 9) analogy." *In re Neurontin Marketing, Sales Practices, and Prods. Liability Litig.*, 612 F.Supp.2d 116, 132–33 (D.Mass.2009) (internal citations omitted); *In re Celexa & Lexapro Prod. Liab. Litig.*, 927 F. Supp. 2d 758, 766 (E.D. Mo. 2013).

occupational NDMA and certain forms of cancer to be irrelevant to general causation. (Def Br. at 12). Defendants also states that “a mere association or correlation between an alleged exposure and a type of cancer is not evidence of causation.” *Id.* This is a massive oversimplification of the scientific methodology used to establish evidence of causation. Defendants are correct to state that a mere association in a single study is not enough to provide evidence of causation. However, Dr. Madigan did much more than just recite the repeated correlations observed in studies, he calculated the lifetime cumulative exposure, dose-response, and strength of association for each epidemiological study.

Defendants’ reliance on *Peters v. AstraZeneca LP*, 224 F. App’x 503, 507 (7th Cir. 2007) and *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 885 (10th Cir. 2005) is unpersuasive, in part because Dr. Madigan considered a glut of evidence, while there was a lack of evidence considered in the aforementioned cases. To compare Dr. Madigan’s thorough, multifactorial analysis on numerous studies with cases such as *Peters*, in which a comparable multifactorial analysis is not addressed, is as misleading as it is flawed.

2. Dr. Madigan’s Methodology was Thorough and Reliable

a. Dr. Madigan’s Analysis was Scientific and Driven by Principles of Data Analysis, Not Litigation

Defendants claim that Dr. Madigan “simply hitched his wagon to the literature supplied by Dr. Etminan and Plaintiffs’ counsel, without conducting any independent research to verify whether there were other data points outside of the universe provided by Etminan that might influence his conclusions.” (Def. Br. at 16). Defendants’ claim is fundamentally untrue. In Dr. Madigan’s deposition, he testified:

So I was asked to review the studies that Dr. Etminan -- that came out of Dr. Etminan's search. They're the ones I reviewed. Now, as we discussed, **I did some of my own**

searching as well. I searched to see was there anything -- any update for Song.⁶ I also looked -- as I read through the papers, **I looked to see were there references to other studies that were missed.** There weren't.

(Madigan Dep. at 71:6-16 (emphasis added)). Subsequent testimony further confirmed this:

Q: And I think you said that in addition to just reading the Zheng paper, **you would have gone on and read the references to this paper,** correct?

A: **To see if there were – if they quantified NDMA** – not nitrates or nitrites, but NDMA and/or NDEA, whether they quantified it and quantified the effect sizes.

(Madigan Dep. at 265:7-14 (emphasis added)).

Further disproving Defendants' claim that Dr. Madigan undertook no independent assessment of the literature, when asked by Defendants "Why did you look at the *Pottegard* paper?", Dr. Madigan replied "Because it pertained broad strokes to the topic I was studying here." (Madigan Dep. at 142:4-7). Thus, Dr. Madigan's testimony clearly demonstrates that he indeed searched for other relevant materials and reviewed additional literature to ensure that Dr. Etminan had not missed anything.

Moreover, in addition to Dr. Madigan's literature search, he also thoroughly investigated the peer reviewers of the *Pottegard* study. (Madigan Dep. at 144:20-23). When discussing the deficiencies of *Pottegard's* methodology, Dr. Madigan explained that his critiques were echoed by peer reviewers. (Madigan Dep. at 143:2-145:16). This statement is not only evidence of Dr. Madigan's independent research, but evidence of Dr. Madigan integrating his independent research into his own analysis. Defendants' contention that Dr. Madigan's expert report was conclusion driven fails for this reason.

b. The Two Cases Cited by Defendants Are Not Applicable to this Case

Of the many cases in which Dr. Madigan has qualified to testify, Defendant's cherry-pick two unanalogous cases in order to prove their predetermined notion that Dr. Madigan is not

⁶ Song is a meta-analysis (attached hereto as **Exhibit L**).

qualified to give his expert opinion; *In re Accutane Litig.* and *In re Incretin-Based Therapies Prods. Liab. Litig.*⁷

In re Accutane Litig. is not analogous or applicable to the case at bar due to the differing methodologies used therein. In *Accutane*, the trial court disqualified Dr. Madigan's expert opinion largely on his failure to complete a meta-analysis of the risk assessment studies.⁸ This situation differs greatly from the present case, in which Dr. Madigan states both in his expert report and his deposition that he considered meta-analyses when coming to his conclusion. Dr. Madigan states in his report that "I considered relevant meta-analyses as well as specific individual studies considering dietary NDMA and its relationship to different cancers." (Madigan Report at 3, attached hereto as **Exhibit B**). Specifically, Dr. Madigan discusses a "2015 meta-analysis by Song et al. included 11 studies concerning NDMA and gastric cancer." (Madigan Report at 3). Dr. Madigan also references the Cui meta-analysis⁹ in his expert report, stating that the "2016 meta-analysis by Cui et al. found an increased risk of esophageal cancer associated with NDMA." (Madigan Report at 4). Additionally, Dr. Madigan incorporates his own meta-analysis into his expert report, stating that "[f]or gastric cancer, both the published meta-analysis and my meta-analysis show a statistically significant increased risk with the largest risks occurring in the two studies with the greatest lifetime." (Madigan Report at 5). As demonstrated

⁷ It's important to note that Dr. Madigan has been successfully qualified by courts to offer his statistical expertise in a variety of cases, including: *In re Taxotere (Docetaxel)*, *Ingham v. Johnson & Johnson*, *Abilify MDL*, *Rheinfrank v. Abbott Labs., Inc.*, *In re Actos* (in three separate cases), *In re Fosamax*, and *In re Yasmin & Yaz (Drospirenone) Mktg., Sales Practices*.

⁸ "Rather than conducting a meta-analysis himself of all the risk assessment studies, and possibly getting "closer to the truth," he chose to disregard eight of them. In doing so, he ignored the knowledge learned from studying approximately 2,100,000 subjects. Instead, he relies upon a study comprised of 509 people." *In re Accutane Litigation*, No. 271(MCL), 2015 WL 753674, at *19 (N.J.Super.L. Feb. 20, 2015) (attached hereto to as **Exhibit I**).

⁹ Attached hereto as Exhibit N.

by the numerous examples above, the underlying issues that formed the basis for excluding Dr. Madigan in *Accutane* are not at all present here.

In re Incretin-Based Therapies Prods. Liab. Litig. is similarly misapplied by Defendants. The *Incretin* court noted that “Dr. Madigan's analysis was limited to a small universe of data provided to him...[h]e did not conduct a comprehensive search of the published peer-reviewed literature for studies evaluating whether incretin-based drugs are associated with an increased risk of pancreatic cancer, and thereby disregarded independent research at odds with his testimony.” *In re Incretin-Based Therapies Prod. Liab. Litig.*, 524 F. Supp. 3d 1007, 1037 (S.D. Cal. 2021). However, with regard to NDMA or NDEA, Dr. Madigan testified that he did conduct a literature search of the published peer-reviewed literature:

Q: If I reference independent research, I mean you, Dr. Madigan, actually doing a PubMed search or some sort of search in a literature database yourself as opposed to being provided documents by counsel. Do you follow?

A: Yeah, I do.

Q: Okay. So assuming that to be the case, did you do any independent research in the case during the course of your review?

A: **I have done some what you're calling independent research, yes, I've done some work along those lines.**

Q: What databases did you use to perform that research?

A: So what's coming to mind is, in particular, I looked at -- the Song meta-analysis was done in 2015, so I ran -- **I did do a search to see was there anything since then that fit the criteria** described in Song. I used the same databases that Song describes, the same search.

Q: Did your search generate any new material or studies?

A: It generated -- the search produced a bunch of studies, I don't know, 50 or something, but none of them -- again, I went through them. None of them were -- were appropriate to include or relevant.¹⁰

¹⁰ Madigan Dep. at 49:13-50:18.

Dr. Madigan conducted a literature review in this case; therefore, *In re Incretin-Based Therapies* is not on point.

Defendants have cherry-picked two cases in which Dr. Madigan, an experienced statistician with years of admissible expert testimony experience, was excluded for aspects of his analysis that are not repeated here, in an attempt to provide a basis for his exclusion in this case. To do so, Defendants resort to twisting the facts of the two aforementioned cases to fit the present case. However, the cases cited by Defendants are simply not comparable: Meta-analyses were conducted by Dr. Madigan in this case, unlike in *In re Accutane Litig.*; Independent research was completed by Dr. Madigan in this case, unlike in *In re Incretin-Based Therapies Prod. Liab. Litig.* As such, any attempts to equate these cases to the current case are disingenuous and must fail.

3. Dr. Madigan did Not Ignore Epidemiologic Literature that Contradicted his Opinion

Defendants' misrepresentations continue in their assessment of Dr. Madigan's treatment of the flawed studies, *Pottegard*¹¹ and *Gomm*.¹² Defendants take issue with Dr. Madigan not including these poorly designed studies in his analysis. However, contrary to Defendants' assertions, Dr. Madigan analyzed every study in which NDMA or NDEA are reasonably quantified, because quantifying the amount of exposure is paramount to his statistical analysis. (See Madigan Dep. at 143:2-146:8). Dr. Etminan reiterates the importance of quantifying exposure for such an analysis with respect to *Pottegard*:

Q: So both of these studies are evaluating the exposure that's actually at issue in this litigation, right, which is exposure to valsartan that contains some small amount of NDMA's of impurity, right?

¹¹ Attached hereto as **Exhibit O**.

¹² Attached hereto as **Exhibit M**.

A: They're not -- I disagree. They're not -- they're not quantifying the NDMA valsartan. They are only looking at valsartan tablets and doses.

Q: The exposure that they're evaluating is -- so the title of the *Pottegard* study is "Use of N-nitrosodimethylamine (NDMA) Contaminated Valsartan Products and Risk of Cancer: Danish Nationwide Cohort Study," right?

A: That -- that is the title, but if you read the study -- the exposure that we're here today to talk about is NDMA and its risk of cancer, and so the study should address the amount of NDMA in valsartan and its risk with cancer. What it does, though, is look at valsartan tablets that have some NDMA in it, in them, we don't know how much. And with respect to *Pottegard*, we -- we are not even sure if the -- the control valsartan group didn't have NDMA in those formulations. So there is definitely measurement error going on in quantifying -- appropriately quantifying NDMA in valsartan along with other limitations.¹³

Defendants inaccurately frame the *Pottegard* study as contradictory to the conclusion that Dr. Madigan eventually formed. However, it is scientifically impracticable for *Pottegard* to be analyzed against the other studies Dr. Madigan considered as it lacked an essential requirement: quantifying the amount of NDMA. The deficiencies with these studies are also noted by Dr. Panigrahy¹⁴ and Dr. Etminan.¹⁵

Defendants claim in their brief that Dr. Madigan, in not performing direct statistical analyses on the *Pottegard* paper, is the same flaw that caused him to be excluded in *In Re Incretin*. This misstates the holding and reasoning of *In Re Incretin*. In holding that Dr. Madigan's testimony should be excluded, the *In re Incretin* court stated that "Dr. Madigan offered **no meaningful explanation as to why** he did not search for or consider these studies other than to say, 'It was not what I was asked to do.'" *In re Incretin-Based Therapies Prod. Liab. Litig.*, 524 F. Supp. 3d 1007, 1037 (S.D. Cal. 2021). As discussed previously, Dr. Madigan

¹³ Etminan Dep. at 266:22 -267:24.

¹⁴ Panigrahy Dep. at 571:9-16.

¹⁵ Etminan Rep. at 24-26.

did not include the *Pottegard* or *Gomm*, because they did not quantify the amounts of NDMA or NDEA that subjects were exposed to when ingesting valsartan.

Dr. Madigan did not ignore *Pottegard* and *Gomm*. Rather, he provided a viable and reasonable explanation, based in biostatistical fundamentals, for excluding *Pottegard* and *Gomm*. Defendants state that “Dr. Madigan’s knowing reliance on cherry-picked literature while disregarding the two most salient pieces of medical literature confirm his opinions are conclusion-driven and wholly unreliable.” (Def. Br. at 20). In reality, what Defendants describe as “salient pieces of medical literature” do not even attempt to quantify the amounts of NDMA or NDEA exposure as a result of ingesting potentially contaminated Valsartan. Because of this fatal flaw, these studies do not provide the information needed by Dr. Madigan in forming any opinion relevant to dose-response, strength of association, or lifetime cumulative exposures, all of which require quantification of exposure.

4. Dr. Madigan Properly Relied on Dr. Panigrahy’s Research that Equated Inhaled and Orally Ingested NDMA

While experts may not simply “parrot” the opinion of other experts, they “are permitted to rely on materials used by other experts in developing their own opinions.” *Leese v. Lockheed Martin Corp.*, 6 F. Supp. 3d 546, 553 (D.N.J. 2014) (*quoting I.B.E.W. Local Union 380 Pension Fund v. Buck Consultants*, No. 03–4932, 2008 WL 2265269, at *3 (E.D.Pa. June 3, 2008)(attached hereto as **Exhibit H**). Experts may also use “a mix of objective data and subjective analysis from another expert to ... create an admissible report,” and the testifying expert's knowledge regarding the underlying facts “go[es] to the weight accorded to [that expert's] report and testimony, rather than its admissibility.” *Id.* Additionally, it is well-settled law that one expert may rely upon another expert's opinion in formulating his own. *Carnegie Mellon Univ. v. Marvell Tech. Grp., Ltd.*, 286 F.R.D. 266, 271 (W.D. Pa. 2012); *Dura Auto. Sys.*

of Indiana, Inc. v. CTS Corp., 285 F.3d 609, 612 (7th Cir. 2002). Experts may also rely on a wide variety of sources when developing an expert opinion. *Ford v. Ford Motor Co.*, 311 F. Supp. 3d 667, 676 (D.N.J. 2017).

Defendants claim that Dr. Madigan simply parroted the opinions of Dr. Panigrahy when he actually relied on Dr. Panigrahy's scientific opinion that NDMA and NDEA are similarly carcinogenic via both inhalation and oral ingestion. (Def. Br. at 21; Madigan Rep. at 32). This is a distortion of Dr. Madigan's methodology. Experts are permitted to rely on opinions reached by other experts when developing their own opinions per *Leese*, which is precisely what Dr. Madigan did.

Dr. Panigrahy routinely works with experts in Dr. Madigan's field, and such experts routinely rely on Dr. Panigrahy's knowledge and expertise.¹⁶ Dr. Madigan is not a medical doctor, and he disclaims any medical expertise at multiple points in his deposition. Dr. Panigrahy, however, has expertise in angiogenesis and its relation to cancer-development, the development of anti-cancer drugs, and various other areas of cancer-biology. (Panigrahy Rep. at 1). Dr. Panigrahy's laboratory has also published seven papers in high impact journals in the field of inflammation resolution in cancer. (Panigrahy Rep. at 3). This is why Dr. Madigan defers to Dr. Panigrahy's exposure assessment (rather than conducting such an assessment himself) in order to translate the amount of inhaled NDMA into the equivalent amount of orally ingested NDMA.

¹⁶ Dr. Panigrahy:" I work with statisticians every day. We translate preclinical drugs to the clinic and we work with epidemiologists and statisticians to design clinical trials for cancer. That's what we do. We translate our preclinical findings to the clinic every day and I'm actively involved with other biostatisticians and clinical translation of cancer drugs." (Panigrahy Dep at 567:22-568:4).

Dr. Panigrahy's work and research is not only relied on by others in his field, but highly acclaimed as well. As such, Dr. Madigan is permitted to rely on his expert opinion in the field of medicine when forming his own opinion in the field of biostatistics. Dr. Madigan is not required to independently conduct research in a field that he is not qualified, and in fact such an undertaking by someone without experience in the field of cancer-biology would be improper. Dr. Madigan properly relied on Dr. Panigrahy's expert medical opinion in developing his own expert biostatistical opinion.

5. The Lifetime Cumulative Exposure Theory Has Been Declared as Reliable by Federal Courts, and Admissible in the District of New Jersey

Defendants allege the lifetime cumulative exposure theory is unreliable, and cite a small collection of cases, all of which are not from the Third Circuit. A deeper look at their research proves their argument to be faulty. Defendants confuse the "each and every exposure" theory with the "lifetime cumulative exposure" theory. Some courts treat these theories as synonymous, however, in this case they are not, and they should not be used interchangeably. *See Coffin v. AMETEK, Inc.*, No. 2:18-CV-472-NT, 2020 WL 5552113 (holding that the "each and every breadth" and "cumulative exposure" theories are not synonymous and that cumulative exposure theories are reliable)(attached hereto as **Exhibit E**).¹⁷

a. Lifetime Cumulative Exposure is Distinguishable from "Each and Every Breath" Exposure

It is important to understand the difference between these two theories. The "each and every breath" argument essentially theorizes that each and every exposure to NDMA or NDEA is a substantial factor in causing cancer. That is not what Dr. Madigan is opining. Rather, Dr. Madigan is providing a calculation, or the threshold amount of NDMA or NDEA exposure that is associated with an increased risk of cancer, based on the literature he reviewed. While every

exposure to NDMA or NDEA does bring the subject closer to the requisite cumulative threshold, the lifetime cumulative exposure theory does not assert that every exposure is significant enough to be a substantial contributing factor in cancer development (as the “each and every breath” theory does). Traditionally, the “each and every breath” theory has been applied to asbestos exposure and mesothelioma cases, in which “the experts explicitly stated that the precise **amount of exposure was not relevant** and that **every exposure should be considered a cause**, ‘regardless of the type of mesothelioma, the exposure ‘dose,’ the type of asbestos, or the passage of time.’”¹⁸ Dr. Madigan offers no such opinions, rather Dr. Madigan and all of Plaintiffs’ experts agree that the amount of NDMA or NDEA exposure is relevant in this case.

b. Lifetime Cumulative Exposure Has Been Admitted in Other Courts

The cumulative exposure theory has been admitted in various circuits, including in the First Circuit in the aforementioned *Coffin* case,¹⁹ and the Second Circuit in *Berman v. Mobil Shipping & Transportation Co.*, No. 14 CIV. 10025 (GBD), 2019 WL 1510941 (S.D. N.Y. 2019)(stating that Courts have found that such a cumulative exposure theory is sufficiently reliable to meet the admissibility standard of Rule 702)(attached hereto as **Exhibit D**). Additionally, the Middle District of Pennsylvania recently ruled that the “cumulative theory of exposure” (which was distinguished from the “each and every breath theory) has been found

¹⁸ In *Coffin*, the Court noted, “Some courts have also rejected a distinction between the “each and every” exposure and “cumulative” exposure theories. *See Rockman v. Union Carbide Corp.*, 266 F. Supp. 3d 839, 849 (D. Md. 2017); *Suoja v. Owens-Illinois, Inc.*, 211 F. Supp. 3d 1196, 1207–08 (W.D. Wis. 2016). But in those cases, the experts explicitly stated that the precise amount of exposure was not relevant and that every exposure should be considered a cause, “regardless of the type of mesothelioma, the exposure ‘dose,’ the type of asbestos, or the passage of time.” *Rockman*, 266 F. Supp. 3d at 848–49.” *Coffin v. AMETEK, Inc.*, No. 2:18-CV-472-NT, 2020 WL 5552113 at fn 7. Dr. Madigan does not go so far in his conclusions in this case.

¹⁹ *Coffin v. AMETEK, Inc.*, No. 2:18-CV-472-NT, 2020 WL 5552113.

reliable by numerous Pennsylvania and federal courts.”²⁰ *Gorton v. Air & Liquid Sys. Corp.*, No. CV 1:17-1110, 2020 WL 4193649, at *2 (M.D. Pa. July 21, 2020) (citing to *Rost v. Ford Motor Company*, 151 A.3d 1032, 1045 (2016) (holding that expert testimony was reliable because it relied on the “ ‘irrefutable scientific fact’ that **every exposure cumulatively contributes to the total dose** (which in turn increases the likelihood of disease)” (attached hereto as **Exhibit F**)).

Further, Defendants’ reliance on *Hoffeditz v. AM Gen., LLC* to exclude Dr. Madigan’s reliance on Dr. Panigrahy’s cumulative exposure is misguided because the expert in *Hoffeditz* was actually *permitted* to testify on that theory. The Court reasoned:

“That while expert testimony based upon the notion that ‘each and every breath’ of asbestos is substantially causative of mesothelioma will not suffice to create a jury question on the issue of substantial factor causation, **the law does not preclude experts from testifying that every exposure [to asbestos] cumulatively contributes to the total dose.**”

Hoffeditz v. AM Gen., LLC, No. CV 09-0257, 2017 WL 3332263, at *2 (D.N.J. Aug. 4, 2017) (internal citations omitted) (emphasis added) (attached hereto as **Exhibit G**). In this case, Dr. Madigan is not relying on an “each and every breath theory,” but is simply relying on Dr. Panigrahy’s opinion that each exposure to NDMA or NDEA contributes to the total dose. The lifetime cumulative exposure theory has been accepted by numerous federal courts, including courts within this very circuit, and therefore does not support exclusion of Dr. Madigan or Dr. Panigrahy.

6. Dr. Madigan’s Final Conclusion was Guided by his Reliable Methodology and Contained No Unfounded Inferential Leaps

²⁰ See also *Rabovsky v. Air & Liquid Systems Corp.*, Civ. Action No. 10-cv-03202, 2012 WL 252919, at *4 (E.D. Pa. Jan. 25, 2012) (attached hereto as **Exhibit J**); *Anderson v. Saberhagen Holdings, Inc.*, Civ. Action No. 10-cv-61118, 2011 WL 605801, at *6 (E.D. Pa. Feb. 16, 2011), (attached hereto as **Exhibit C**).

Defendants take issue with the final paragraph of Dr. Madigan's report, which states the following:

Based on valsartan dosing, the levels of NDMA reported in contaminated valsartan and the timeframe over which the contamination occurred, it is scientifically plausible that users of contaminated valsartan could develop cancer. For example, in one year, a daily user of valsartan contaminated with 20 µg of NDMA would reach cumulative exposures for which both Hidajat et al. and several dietary studies show statistically significantly elevated risks of several cancers. Including NDMA from other sources would shorten this time further.

(Def. Br. at 25).

Specifically, Defendants assert that because Dr. Madigan does not explain what he means by "valsartan dosing" or the "timeframe over which the contamination occurred" that his opinion makes an unfounded inferential leap. (Def. Br. at 25). In the section of his expert report titled "Introduction", Dr. Madigan explains the levels of NDMA or NDEA that can be found in a dose of valsartan:

Levels of NDMA in contaminated valsartan tablets range from below the limit of detection to 20.19 µg while levels of NDEA in contaminated valsartan tablets range from below the limit of detection to 1.31 µg. Other sources show levels as high as 60.2 µg of NDMA and 5.4 µg of NDEA.

(Madigan Rep. at 2). For support that contaminated valsartan contains levels of NDMA up to 20.19 µg, Dr. Madigan initially cited to a 2019 article by Snodin²¹ titled Short Commentary on NDMA Contamination of Valsartan Products, which also explains when the contamination likely started:

Zhejiang Huahai modified the existing chemistry during the **period between 2011/2013** by replacing tributyltin azide with the more reactive sodium azide as a reagent used in the formation of a tetrazole ring structural moiety, which necessitated the introduction of NaNO₂ to remove excess azide reagent. However, under acidic conditions nitrite can also form nitrous acid. It would appear that impurities in the solvent DMF (dimethylformamide) particularly dimethylamine, but also diethylamine, reacted with nitrous acid (a nitrosating agent) to yield

²¹ Attached hereto as **Exhibit P**.

NDMA (or NDEA)... Regulatory questions now appear to be focused on this mechanistic explanation

Dr. Madigan then cited the FDA's website as further support as to the amount of NDMA or NDEA found in a dose of valsartan. The FDA's website also discusses the likely timeframe over which the contamination occurred, noting "[b]ased on FDA laboratory testing results and records from manufacturers of the recalled valsartan lots, the impurities may have been present in valsartan-containing finished drug lots for up to four years (emphasis added)."²² For the higher levels of NDMA (60.2 µg) and NDEA (5.4 µg), Dr. Madigan cited internal documents from ZHP, Solco, and Torrent. Defendants questioned Dr. Madigan at length on his citation to Snodin and the FDA's website. (Madigan Dep. at 124:9-133:1). Defendants even questioned Dr. Madigan on what he meant by "timeframe over which the contamination occurred", to which Dr. Madigan explained that as he understood it, "in some cases people were consuming these tablets for years, these contaminated tablets for years. That's my understanding." (Madigan Dep. at 211:23-212:10). Defendants then asked Dr. Madigan if he knew the exact number of years, to which he candidly replied, "I don't. But years – small number of years is enough to get to the levels in some of these studies. That is my – I don't know the exact number of years." (Madigan Dep. at 212:12-17). As evidenced by the sources Dr. Madigan cited to, there is some ambiguity as to how long valsartan has been contaminated with NDMA.

Defendants mischaracterize portions of Dr. Madigan's deposition in order to make the argument that his conclusion contained an inferential leap. Defendants also take issue with the following statement from Dr. Madigan:

I mean -- you know, I studied across a variety of dietary studies, and significant occupational study, and the association between certain amounts of cumulative

²² <https://www.fda.gov/drugs/drug-safety-and-availability/laboratoryanalysis-valsartan-products>.

exposure to NDMA and cancer outcomes, and, you know, in many cases, there are statistically significant associations, you know, between them. And so, you know, **if indeed these levels of NDMA -- in these studies if indeed they cause cancer**, this is exactly what you'd expect to see. These kinds of associations are exactly what you'd expect to see. And based on this analysis, it seems entirely plausible to me that user -- **based on what I know about the contamination levels in valsartan, it's entirely plausible to me** that the contaminated valsartan -- those folks could have developed -- the folks that took contaminated valsartan could have developed cancer.

(Def. Br. at 26; Madigan Dep. 208:9-209:5). Defendant's frame Dr. Madigan's first bolded statement ("if indeed these levels of NDMA -- in these studies if indeed they cause cancer") as a starting point for his analysis. This is not a correct reading of his statement. Dr. Madigan makes a point to use "if" not once, but twice in this statement. Dr. Madigan also makes a point to not conclude that valsartan causes cancer, but to state that based on the contamination levels he's discerned from his *statistical research*, that it would be "entirely **plausible**" that valsartan causes cancer. These are not conclusory statements regarding causation as it relates to valsartan and cancer. These are statements describing the endpoint of his data collection and analysis. Stating that the results of a statistical analysis leans in the favor of one conclusion is not the equivalent of actually making that conclusion. Further, stating that causation is *plausible* is not the same as stating that a situation is *currently present or applicable*.

Defendants play free and loose with the definitions of the words in their argument in order to attempt to paint Dr. Madigan's testimony as conclusions regarding medical causation and not a biostatistical analysis. This false equivalency between medical and statistical expertise is one that Defendants often attempted in their brief, and this disingenuous interpretation of Dr. Madigan's statements is no different. Dr. Madigan did not embark on a conclusion-based analysis and his testimony should be admitted.

Defendants' erroneously represent that Dr. Madigan's reliance on dietary and occupational studies is improper. Def. Brief at 26. Defendants cite *Gen. Elec. Co. v. Joiner* in

support.²³ However, the Third Circuit has emphasized that District Courts should take care not to “mistake credibility questions for admissibility questions.” *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 157 (3d Cir. 1999). Regarding credibility versus admissibility, this court also held that “even absent hard evidence of the level of exposure to the chemical in question, a medical expert could offer an opinion that the chemical caused plaintiff’s illness” and that if a “medical expert’s opinion on causation has a *factual basis and supporting scientific theory that is reliable, it should be admitted.*” *Id.*

Defendants claim Dr. Madigan “does not explain why dietary and occupational exposure evaluating NDMA exposures in food or air supply are relevant to the question at issue”, which Defendants narrowly frame as “whether pharmaceutical exposure to NDMA or NDEA is capable of causing the specific cancers Plaintiffs allege.” (Def. Br. at 27). This is patently false, as Dr. Madigan states that he relied on any studies that quantified NDMA or NDEA ingestion and then compared those cumulative exposures levels to the potential cumulative levels Plaintiffs were exposed to as a result of NDMA being present in valsartan. (Madigan Dep. at 196:18-20; 265:11-14). While it is true that Plaintiffs NDMA exposure was via contaminated pharmaceuticals, the relevant inquiry is the relation between ingestion of quantified amounts of NDMA and their causal effects on various cancers.

Contrary to Defendants assertions, Plaintiffs own experts have not conceded that dietary and occupational exposures are not the relevant inquiry, or that they are “notoriously unreliable.” (Def. Br. at 27). Instead, Dr. Etminan acknowledged that the potential for inaccurate reporting “could occur in any dietary study.” (Etminan Dep. at 142:12-20). Dr. Hecht similar acknowledged, “Well, you know, just about all of these studies can be criticized for one reason

²³ 522 U.S. 136, 146, 118 S. Ct. 512, 519, 139 L. Ed. 2d 508 (1997).

or another.” (Hecht Dep. at 217:18-20). Setting aside the fact that Defendants attack on the strength of the studies underlying Plaintiffs experts’ opinions goes to the weight, and not the admissibility of those opinions, Dr. Etminan actually accounted for the potential weaknesses in these studies. For instance, Dr. Etminan calculated the magnitude of effect that an unmeasured confounder would have to achieve to reverse the identified increased risk found in the study. (Etminan Report at 15).

Defendants do not offer any scientific reason in their brief for why dietary or occupational ingestion of a certain amount NDMA would result in a different outcome than if the same amount of NDMA was ingested via a pharmaceutical. Defendant’s position seems to be that *any* bias or confounding variables in a study automatically disqualifies it from consideration, even if adjusted and accounted. The problem with this approach is that would also invalidate the two studies they criticize Dr. Etminan and Dr. Madigan for excluding, *Pottegard*²⁴ and *Gomm*.²⁵ The difference between Dr.

²⁴ “Unlike the study by *Hidajat*, the study by *Pottegard* suffers from inadequate follow up, lack of control for competing events, and misclassification of valsartan tablets that might have had a high NDMA content with those that might have lower amounts. The combination of these factors probably led to false negative results in this study.” Etminan Rep at 25.

²⁵ Another recent study by *Gomm* from Germany also attempted to examine the risk of cancer with valsartan formulations that had different amounts of NDMA. The study was a cohort study that used health records of 25 million subjects with health insurance. Subjects entered the cohort if they filled *one* prescription of valsartan from 2012-2017 and were followed to the first incidence of cancer. The study did not find an overall risk of cancer with NDMA use, but a statistically significant increase in risk with liver cancer was found (HR 1.16; 95% CI: 1.03-1.31) but no risk was detected with 9 other cancers. The study had several limitations which I describe below:

- The major limitation of the study was the median follow up of 3 years which is woefully inadequate to detect all cancer formations that would result from NDMA exposure; The authors implemented up to a two year ‘lag’ in the study meaning cases in the first two years of follow up were excluded as these cases were probably not considered to be linked to NDMA. However, this means that the true follow up to detect cancer was only one year (3 years total follow up minus 2 years lag) post NDMA use which would not be considered sufficient induction time for all cancers to occur; Similar to the *Pottegard* study, the study by *Gomm* could not specifically

Etminan's and Dr. Madigan's exclusion of *Pottegard* and *Gomm* from their analysis and Defendants insistence that dietary/occupational studies be excluded is that Dr. Etminan and Dr. Madigan actually possess a scientific and statistical *reason* for their exclusion, that reason being that lack of quantification of NDMA. Defendants essentially seek to include studies that do not quantify the amounts of NDMA and accept any results of that analysis without adjusting for confounding factors, while simultaneously *excluding studies that have quantified NDMA and properly adjusted the confounding variables*. Defendants' objections to Dr. Madigan's reliance on dietary and occupational studies with quantified amounts of NDMA therefore speak to weight, not admissibility, and should be admitted pursuant to *Heller*.

7. Dr. Madigan's Opinions Regarding NDEA as it Relates to Gastric, Pancreatic, Esophageal, Bladder, Prostate, Lung, and Colorectal Cancers Should be Admitted as He Used Scientific Methodology

Defendants argue that Dr. Madigan's opinions on relationships or associations between NDEA and any type of cancer should be excluded. Defendants' claim should fail for the methodology he used to examine the statistical relationship between certain cancers utilized a reliable methodology.

A trial court will find expert testimony reliable if it is based on "methods or procedures of science" rather than on "subjective belief or unsupported speculation." *Kannankeril* 128 F.3d at 806. Experts use "a mix of objective data and subjective analysis from another expert to ... create an admissible report, and the testifying expert's knowledge regarding the underlying facts go[es] to the weight accorded to [that expert's] report and testimony, rather than its

identify the true NDMA levels of the various valsartan batches, and the dose-response analysis only looked at cumulative dose of valsartan *per se* and not the cumulative NDMA content in the valsartan formulations (mg of pill vs. ng of NDMA in pill)." Etminan Rep. at 26.

admissibility.” *Leese*, 6 F. Supp. 3d at 553 (internal citations omitted). Admissibility determinations are based on the expert’s methods and reasoning, with credibility decisions decided after admissibility has been determined. *Kannankeril* 128 F.3d at 806.

Dr. Madigan’s expert opinion on the relationship between NDEA and pancreatic cancer should be admitted because it was based on reliable scientific methods of biostatistical analysis. Defendants allege that Dr. Madigan, during his deposition, “conceded” that the *Zheng* study²⁶ (on which Dr. Madigan relied to form an opinion regarding NDEA exposure and pancreatic cancer) was “significantly limited.” (Def. Br. at 5). However, Defendants failed to provide any citation to support this claim, likely because this characterization of Dr. Madigan’s testimony is misleading, if not patently false. Dr. Madigan never said that the *Zheng* study is significantly limited in his entire deposition. He actually states that the *Zheng* study, which was a “large hospital-based matched case control study,” found “a biologically plausible cause and association of two potent dietary carcinogens, NDEA and NDMA, with pancreatic cancer.” (Madigan Dep. 266:10-15).

Defendants also claim that Dr. Madigan’s statistical analysis of the *Zheng* study should be excluded because Dr. Madigan did not undertake any independent analysis of NDEA. (Def. Br. at 28). This claim is a repeat of the same false premise that Defendants used repeatedly throughout their brief. Dr. Madigan is not a medical doctor and thusly did not offer medical causation opinions. His expert opinions were of a statistical nature. As such, he was allowed to rely on data and analysis provided by experts in the field to craft his own expert opinion, pursuant to the standard set forth in *Leese v Lockheed Martin*.²⁷ The standard that Defendants are proposing, that a doctor in mathematics and statistics be required to become an expert in each

²⁶ Attached hereto as **Exhibit Q**.

²⁷ *Supra* at 12.

and every field whose statistics he analyzes and then complete independent verifications of each dataset, is misinformed.

Dr. Madigan analyzed the *Zheng* study and the data therein that showed a possible relation between NDEA and pancreatic cancer because it was the only study that quantified the amount of NDEA. (Madigan Dep. at 196:5-7). Dr. Madigan did his due diligence as a biostatistician by examining the forty-three NDEA related references in *Zheng*. (Madigan Dep. 197:1-13). Defendants argue that Dr. Madigan is not qualified to testify on his findings in the *Zheng* study because the study noted that an association between pancreatic cancer and NDEA “needed to be confirmed in a readily large prospective study.” (Def. Br. at 29; Madigan Dep. at 266:20-268:11). Defendants also argue that his testimony should be excluded because his conclusion after analyzing the quantified NDEA amounts was that “it would take you 6,631 days to get to . . . cumulative [NDEA] exposure of 2,520[micrograms]”.²⁸ (Def. Br. at 29; Madigan Dep. at 280:2-9).

What Defendants propose here is to exclude an expert witness, not based on his methodology, but the conclusions that result from his methodology. However, as *Kannankeril* dictated, expert admissibility determinations are based on methodology and reasoning, not the conclusions resulting from those methods. Defendants do not argue that Dr. Madigan undertook a faulty methodology in analyzing the *Zheng* findings. Defendants do not argue that Dr. Madigan used subjective belief or unsupported speculation to come to his conclusions. On the contrary, Defendants take Dr. Madigan’s *Zheng* findings as true, but somehow also argue that those findings render his expert opinion unreliable. This is not the standard under *Kannankeril*

²⁸ 2,520 micrograms is the amount of lifetime cumulative exposure that Dr. Madigan concluded would be needed to spark a significant increase in likelihood of developing pancreatic cancer based on *Zheng*. Madigan Dep. 280:11-13.

and their argument should be rejected. At most, this is a case specific issue to be addressed with individual plaintiffs.

Further, it is important to note that Dr. Madigan's lifetime cumulative exposure thresholds are not bright line measurements. It is possible that consumers of Valsartan could have an increased risk of cancer development at a lower cumulative exposure level than what Dr. Madigan provided, as genotoxic carcinogens such as NDMA and NDEA can cause cancer at any dose.²⁹ Additionally, a person's risk of cancer from NDEA ingestion is additive to their risk of cancer from ingesting NDMA. There is a more than adequate basis to admit the opinions regarding NDEA.

CONCLUSION

Dr. Madigan, a Doctor of Mathematics and Biostatistics, has been qualified by federal courts to offer his expert analysis in his field in many cases over the past decade. Dr. Madigan did not offer medical causation opinions that he was not qualified to give. Rather, he supplied his statistical analysis of the data in order to form a statistical basis for general causation opinions. This approach has been accepted by federal courts and it should be accepted in this case as well. At all times, Dr. Madigan used a reliable scientific method that utilized a mix of independent research, data analysis, and analysis of other expert opinions in their field of expertise and is well qualified under Daubert to offer his expert opinion in these areas. For the aforementioned reasons, this Court should deny the Defendant's motion to exclude, or limit, Dr. Madigan's testimony.

Respectfully,

²⁹ Panigrahy Dep. 44: 13-19.

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Dated: December 1, 2021

CERTIFICATE OF SERVICE

I hereby certify that on December 1, 2021, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notifications of such filing to the CM/ECF participants registered to receive service in this MDL.

/s/ Madeline Pendley

Madeline Pendley